

## RECEIVED APR 0 9 2003 TECH CENTER 1600/2900

Human caspase-13a conserved amino acids<sup>b</sup> Mouse caspase-11 Mouse Human caspase-12 Human caspase-5 Human caspase-4 Human caspase-1 caspase-12

MFKGILQSGLDNFVINHMLKNNVAGQTSIQTLVPNTDQKSTSVKKDNHKKKTVKMLEYLG

----- MAARRTHERDPIYKIKGLA

MAENKHPDKPLKVLEQLG

:

VHMVKLLI

Human caspase-1 caspase-13ª

Human Mouse Mouse Human caspase-11 caspase-5 caspase-12 caspase-12

Human Human

caspase-4

conserved amino acidsb

Human Human Human caspase-1 Mouse Human Human caspase-13ª caspase-5 caspase-12 caspase-12 caspase-4

conserved amino acidsb Mouse caspase-11

Human caspase-1 caspase-13ª

Mouse caspase-11 caspase-12 Human Human Human Human

caspase-12 caspase-5 caspase-4

conserved amino acidsb

KDVLHGVFNYLAKHDVLTLKEEEKKKYYDAKIEDKALILVDSLR-KNRVAHQMFTQTLLN EGTINGLLDELLQTRVLNKEEMEKVKRENATVMDKTRALIDSVIPKGAQACQICITYICE KTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVDDITETAQIAGKIFREHLWN KDFLTGVLDNLVEQNVLNWKEEEKKKYYDAKTEDKVRVMADSMQEKQRMAGQMLLQTFFN KELISGLLDDFVEKNVLKLEEEEKKKIYDAKLQDKARVLVDSIRQKNQEAGQVFVQTFLN

KEVLTEYLEKLVQSNVLKLKEEDKQKFNNAERSDKRWVFVDAMKKKHSKVGEMLLQTFFS KDMLDGVFDDLVEKNVLNGDELLKIGESASFILNKAENLVENFLEKTDMAGKIFAGHIAN .. .. .. .. 

EDSYLAGTLGLSADQ-----TSGNYLNMQDSQGVLSSFPAPQAVQDN-----PAMPTS SQEQLSLQFSNDEDDGPQKICTPSSPSESKRKVEDDEMEVNAGLAHESHLMLTAPHGLQS SKKQES------ID---------PPESG----QKI----TSVKPLLQIEAG----PPESA---KNS----TSIKAPEETVAG-----PDESV---PGS----HHGEANLEMEE-----PEE---

SGSEGNVKLCSLEEAQRIWKQKSAEIYPIMDKSSRTRLALIICNEEFDSIPRRTGAEVDI

SEVQDTLKLCPRDQFCKIKTERAKEIYPVMEKEGRTRLALIICNKKFDYLFDRDNADTDI GSAATLKLCPHEEFLKLCKERAGEIYPIKERKDRTRLALIICNTEFDHMPPRNGAALDI ESTNILKLCPREEFLRLCKKNHDEIYPIKKREDRRRLALIICNTKFDHLPARNGAHYDI ESTDALKLCPHEEFLRLCKERAEEIYPIKERNNRTRLALIICNTEFDHLPPRNGADFDI SLNTLKLCSPEEFTRLCREKTQEIYPIKEANGRTRKALIICNTEFKHLSLRYGAKFDI --- QIYPVMEKERRTCLASNIRNKEFNYLHNRNGSELDI

#### FIGURE 1A

	· was a second conservation	THE PERSON NAMED IN COLUMN TWO IS NOT THE OWNER.	t
		NAMETSARO	
SSAJOBUS	SEA10	BA	
'E:13	9	03: UNSCA	
Accompany of the Contract of t	THE BOARD OF THE PARTY	SAME WASHINGTON AND ADDRESS.	•

----- MAEDKHNKNPLKMLESLG

--- MAEGNHRKKPLKVLESLG

---- MADKVLKEKRKLFIRSMG



conserved amino acidsb Human caspase-13ª Mouse Human Human Human Human caspase-1 caspase-5 caspase-11 caspase-12 caspase-12 caspase-4

Human caspase-13a conserved amino acidsb Mouse caspase-11 Mouse Human caspase-12 Human Human caspase-4 Human caspase-1 caspas e-5 caspase-12

Human caspase-1

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conserved amino acidsb Human Mouse Mouse Human Human Human caspase-11 caspase-12 caspas e-13ª caspase-5 caspase-4 caspase-12

conserved amino acidsb Human caspase-1 Mouse Mouse Human Human Human Human caspas e-13<sup>a</sup> caspase-11 caspase-5 caspase-12 caspase-12 caspase-4

> ${f TGMKELLEGLDY}$   ${f SVDVEENLTARD}$   ${f MESALRAFATRPEHKSSDSTFLVL}$   ${f MSHGILEGICGT}$ LGMKQLLEGLGY TVEVEEKLTARD MESVLWKFAARE EHKSSDSTFLVF MSHGILDGICGT LNMQELLENLGY SVVLKENLTAQE METELMQFAGRP EHQSSDSTFLVF MSHGILEGICGV VGMKRLLQGLGY TVVDEKNLTARD MESVLRAFAARP EHKSSDSTFLVL MSHGILEGICGT TGMTMLLQNLGY SVDVKKNLTASD MTTELEAFAHRP EHKTSDSTFLVF MSHGIREGICGK IGMKGLLEDLGY DVVVKEELTAEG MESEMKDFAALS EHQTSDSTFLVL MSHGTLHGICGT LGMXDLLENLGY SVGIKENLTAQE METALRQFAAHP EHQSSDSTFLVV MSHSILNGICGT \*\* \* \*\*\* \*\*\*\*\*\* \*\*\* . \* \*

\* ..

MHSEKTPDVLQY DTIYQIFNNCHC PGLRDKPKVIIV QACRGGNSGEMW IRESSK-PQLCR MHSEEEPDVLPY DTIFRTFNNRNC LSLKDKPKVIIV QACRGANRGELW VSDSPP-ALADS KHSEQVPDILQLNAIFNMLNTKNC PSLKDKPKVIII QACRGDSPGVVW FKDSVG-VSGNL KHRNKKPDVLHD DTI FKI FNNSNC RSLRNKPKILIM QACRGRYNGTIW VSTNKGIATADT KHWDQEPDVLHD DT1FE1FNNRNC QSLKDKPKV1IM QACRGNGAGIVW FTTDSGKASADT AHKKKKPDVLLY DTI FQI FNNRNC LSLKDKPKVI I V QACRGEKHGELW VRDSPA-SLAV I VHDEKKPDVLLY DTI FQI FNNRNC LSLKDKPKVI I V QACRGANRGELW VRDSPA - SLEVA

FSQ-SSENLEED AVYKTHVEKDFI AFCSSTPHNVSW RDIKKGSLFITR LITCFQKYAWCC GVD-LPRNMEAD AVKLSHVEKDFI AFYSTTPHHLSY RDKTGGSYFITR LISCFRKHACSC HGRLLQGNICND AVTKAHVEKDFI AFKSSTPR----SSQ-SSENLEAD SVCKIHEEKDFI AFCSSTPHNVSWRDRTRGSIFITE LITCFQKYSCCC SSQ-SSENLEED AVYKTHVEKDFI AFCSSTPHNVSWRDSTMGSIFITQ LITCFQKYSWCC SLP-TTEEFEDD AIKKAHIEKDFI AFCSSTPDNVSW RHPTMGSVFIGR LIEHMQEYACSC DEERVLSCKWNN SITKAHVETDFI AFKSSTPHNISW KVGKTGSLFISK LIDCFKKYCWCY \* \* \*\*\*\*

:: ::

HLMEIFRKVQKS FEVPQAKAQMPT IERATLTRDFYL FPGN DVEEIFRKVRFS FEQPDGRAQMPT TERVTLTRCFYL FPGH HLEEIFRKVQHS FEVPGELTQMPT IERVSMTRYFYL FPGN HLEEVFRKVQQS FETPRAKAQMPT IERLSMTRYFYL FPGN HLEEVFRKVQQS FEKPNVKAQMPT VERLSMTRYFYL FPGN HLFDIFLKVQQS FEKASIHSQMPT IDRATLTRYFYL FPGN ---SHS FETPNILTQLPT TERLSMTRYFYL FPGN \*\*\*\*\* \*\* \*\* \*\* \*\* \*\*

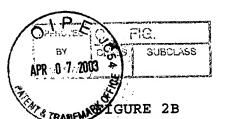
FIGURE 1B

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FIGURE 2	A
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FIGURE 2A	
hCaspase12	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD
KW-Ap	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD
KW-Bp	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAE-LVD
KW-Cp	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD
KW-Dp	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD
KW-Ep	
KW-Fp	
KW-Hp	
KW-Gp	
KW-Ip	
- KW-Jp	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD
KW-Kp	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD
KW-KD	PROBRESHOV BY HE KIT EDGIT DODING MY HAT DEFINE TO KEEK TO VORKEND VO
hCaspase12	DITETAQIAGKIFREHLWNSKKQLSSALLEIQGAQPSGKLKLCPHAHFHELKTKRADEIY
KW-Ap	DITETAQIAGKIFREHLWNSKKQLSSDISSDGEREANMPG
KW-Bp	DITETAQIAGKIFREHLWNSKKQLSSDISSDGEREANMPG
KW-Cp	DITETAQIAGKIFREHLWNSKKQLSSDISSDGEREANMPG
KW-Dp	DITETAQIAGKIFREHLWNSKKQLSSDISSDGEREANMPG
KW-Ep	PSGKLKLCPHAHFHELKTKRADEIY
KW-Fp	AQPSGKLKLCPHAHFHELKTKRADEIY
KW-Hp	AQPSGKLKLCPHAHFHELKTKRADEIY
KW-Gp	AQPSGKLKLCPHAHFHELKTKRADEIY
KW-Ip	AQPSGKLKLCPHAHFHELKTKRADEIY
KW-Jp	DITETAQIAGKIFREHLWNSKKQLSSDISSDGEREANMPG
KW-Kp	DITETAQIAGKIFREHLWNSKKQLSSALLEIQGAQPSGKLKLCPHAHFHELKTKRADEIY
hCaspase12	PVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMRDLLENLGYSVVIKENLTAQEMET
•	
KW-Ap	LNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQEMET
KW-Bp	LNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQEMET
KW-Cp	LNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQ
KW-Dp	LNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQ
KW-Ep	PVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMRDLLENLGYSVVIKENLTA
KW-Fp	PVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKESLTAQEMET
KW-Hp	PVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQ
KW-Gp	PVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQ
KW-Ip	PVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQEMET
KW-Jp	LNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQEME-
KW-Kp	PVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMXDLLENLGYSVVIKENLTAQEMET
	************* ****** ********
hCaspase12	ALRQFAAHPEHQSSDSTFLVFMSHGILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL
KW-Ap	ALRQFAAHPEHQSSDSTFLVFMSHSILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL
KW-Bp	ALRQFAAHPEHQSSDSTFLVFMSHSILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL
KW-Cp	
KW-Dp	
KW-Ep	SILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL
KW-Fp	ALRQFAAHPEHQSSDSTFLVFMSHSILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL
KW-Hp	
KW-Gp	
KW-Ip	ALRQFAAHPEHQSSDSTFLAFMSHSILNRICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL
KW-Jp	STFLVFMSHSILNGICGTKH
UP	
KW-Kp	ALRQFAAHPEHQSSDSTFLVFMSHSILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL



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hCaspase12	$\mathtt{KDKPKVIIMQACRGNGAGIVWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFK}$
ĸw-Ap	KDKPKVIIMQACRGNGAGIVWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFK
KW-Bp	KDKPKVIIMQACRGNGAGIVWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFK
KW-Cp	GAGIVWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFK
KW-Dp	
KW-Ep	KDKPKVIIMQACRG
KW-Fp	KDKPKVI IMQACRGKDKPKVI IMQACKDKPKVI IMQAC
KW-Hp	GAGIVWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFK
KW-Gp	MVLGLFGSP
KW-Ip	KDKPKMVLGLFGSP
KW-Jp	
KWKp	KDKPKVIIMQACRGNGAGIVWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFK
hCaspase12	SSTPHNVSWRHETNGSVFISQIIYYFREYSWSHHLEEIFQKVQHSFETPNILTQLPTIER
<del>-</del>	SSTPHNVSWRHETNGSVFISQIIYYFREYSWSHHLEEIFQKVQHSFETPNILTQLPTIER
KW-Ap	SSTPVQHSFETPNILTQLPTIER
KW-Bp	SSTPHNVSWRHETNGSVFISQIIYYFREYSWSHHLEEIFQKVQHSFETPNILTQLPTIER
KW-Cp	SSTPVQHSFETPNILTQLPTIER
KW-Dp	5517
KW-Ep	
KW-Fp	SSTPHNVSWRHETNGSVFISQIIYYFREYSWSHHLEEIFQKVQHSFETPNILTQLPTIER
KW-Hp	LTVEKPVQILMVGSCKVTSVMMLLQRLMWKRTSLLSNLPHHVQHSFETPNILTQLPTIER
KW-Gp	
KW-Ip	LTWKKPVQILMVGSCKVTSVMMLLQRFMWKRTSLLSNLPHHVQHSFETPNILTQLPTIER
KW-Jp	COMPANY OF THE PROPERTY OF THE
KW-Kp	SSTPHNVSWRHETNGSVFISQIIYYFREYSWSHHLEEIFQKVQHSFETPNILTQLPTIER
•	
hCaspase12	LSMTRYFYLFPGN
KW-An	I.SMTRYFYLFPGN

hCaspase12	LSMTRYFYLFPGN
KW-Ap	LSMTRYFYLFPGN
KW-Bp	LSMTRYFYLFPGN
KW-Cp	LSMTRYFYLFPGN
KW-Dp	LSMTRYFYLFPGN
KW-Ep	
KW-Fp	
KW-Hp	LSMTRYFYLFPGN
KW-Gp	LSMTRYFYLFPGN
KW-Ip	LSMTRYFYLFPGN
KW-Jp	
KW-Kp	LSMTRYFYLFPGN



Human Caspase-12 compared to Mouse Caspase-12 with CARD domain, ICE-p20 domain, ICE-p10 domain and Active-site amino acids described.

hCaspase-12 mCaspase-12	MADEKPSNGVLVHMVKLLIKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD MAARRTHERDPIYKIKGLAKDMLDGVFDDLVEKNVLNGDELLKIGESASFILNKAENLVE ** .:. : : : * * * :***: **** **: **:*::.:*****:	60
hCaspase-12 mCaspase-12	DITETAQIAGKIFREHLWNSKKQLS	85 120
hCaspase-12 mCaspase-12	AGLAHESHLMLTAPHGLQSSEVQDTLKLCPRDQFCKIKTERAKEIYPVMEKEGRTRLALI  *	134 180
hCaspase-12 mCaspase-12	IRNKEFNYLHNRNGSELDLLGMRDLLENLGYSVVIKENLTAQEMETALRQFAAHPEHQSS ICNKKFDYLFDRDNADTDILNMQELLENLGYSVVLKENLTAQEMETELMQFAGRPEHQSS * **: *: **: * : *: * : * : * : * * * *	194 240
hCaspase-12 mCaspase-12	DSTFLVFMSHGILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSLKDKPKVIIMQACRG DSTFLVFMSHGILEGICGVKHRNKKPDVLHDDTIFKIFNNSNCRSLRNKPKILIMQACRG ************************************	254 300
hCaspase-12 mCaspase-12	NGAGI VWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFKSSTPHNVSWRHETN RYNGT IWVSTNKGIATADTDEERVLSCKWNNSITKAHVETDFIAFKSSTPHNISWKVGKT * :*:*********************************	314 360
hCaspase-12 mCaspase-12	GSVFISQIIYYFRBYSWSHHLEBIFQKVQHSFETPNILTQLPTIERLSMTRYFYLFP GN GSLFISKLIDCFKKYCWCYHLBBIFRKVQHSFEVPGBLTQMPTIERVSMTRYFYLFP GN **:***::*	373 · . 419

#### FIGURE 3

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		AAN COMPA	:
SCALOBUS	CLA55	BA	
:le:		0340,1414	,



h_Caspase-3 h_Caspase-7	h_Caspase-8 h_Caspase-10 h_Caspase-9 h_Caspase-2 h_Caspase-14	h_Caspase-12 m_Caspase-12 m_Caspase-12 h_Caspase-13 h_Caspase-13 h_Caspase-5 h_Caspase-1	h_Caspase-9 h_Caspase-10 h_Caspase-9 h_Caspase-2 h_Caspase-14 h_Caspase-14	rigure 4A  h Caspase-3 h Caspase-7 h Caspase-12 m Caspase-12 h Caspase-4 h Caspase-13 h Caspase-13 h Caspase-1
MADDQGCIEEQGVEDSANEDSVDSK-SIKNLEPKIIHGSE	KEEMERELQTPGRAQ KEEVERLLPTRQR PHMIEDIQRAGSGSR LEMRELIQAKVGS		MKSQGQHWYSSSDKNCKVSFREKLLIIDSNLGVQDVENLKFLCIGLVPNKKLEKSSSASD	VINHMLKNNVAGQTSIQTLVPNTDQKSTSV

		MANASLAVIO	
SSAUDEUS	CLASS	УВ	
:i3'	F = 0	GENOR-4A	



h_Caspase-4	h_Caspase-3 h_Caspase-7 h_Caspase-12 m_Caspase-12	h_Caspase-12 h_Caspase-12 m_Caspase-12 h_Caspase-1 h_Caspase-13 h_Caspase-5 h_Caspase-6 h_Caspase-6 h_Caspase-6 h_Caspase-8 h_Caspase-9 h_Caspase-10 h_Caspase-10 h_Caspase-14	2 14 2 0 0 0 1 5 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
IYPIKERNNRTRLALIICN		DDEMEVNAGLAHESHLMLTAPHGLQSSEVQDTLKLCPRDQFCKIKTERAKE	LVDDITETAQIAGKIFREHLWNSKKQLSSALLEIQGAQPSGK LVENFLEKTDMAGKIFAGHIANSQEQLSLQFSNDEDDGPQKICTPSSPSESKRKV MADSMQEKQRMAGQMLLQTFFNIDQISPNKKAHPNMEAGPPESGES LVDSIRQKNQEAGQVFVQTFLNIDQKITSVKPLLQIEAGPPESVGS LVDSLR-KNRVAHQMFTQTLLNMDQKITSVKPLLQIEAGPPESAES LIDSVIPKGAQACQICITYICEEDSYLAGTLGLSADQTSGNYLNMQDSQGVLSSFPA





h_Caspase-3 h_Caspase-7 h_Caspase-12 m_Caspase-12 h_Caspase-4 h_Caspase-4	h_Caspase-3 h_Caspase-7 h_Caspase-12 m_Caspase-12 h_Caspase-13 h_Caspase-5 h_Caspase-6 h_Caspase-6 h_Caspase-6 h_Caspase-10 h_Caspase-10 h_Caspase-9 h_Caspase-2 h_Caspase-14	FIGURE 4C h_Caspase-13 h_Caspase-5 h_Caspase-6 h_Caspase-6 h_Caspase-10 h_Caspase-10 h_Caspase-9 h_Caspase-2 h_Caspase-14
DHSKRSSFVCVLLSHGEEGIIFGTNGPVDLKKITNFFRGDRCRSL DHTNAACFACILLSHGEENVIYGKDGVTPIKDLTAHFRGDRCKTL EHQSSDSTFLVFMSH_GILNGICGTKHWDQEPDVLHDDTIFEIFNNRNCQSL EHQSSDSTFLVFMSHGILEGICGTVHDEKKPDVLHDDTIFKIFNNSNCRSL EHKSSDSTFLVLMSHGILEGICGTVHDEKKPDVLLYDTIFQIFNNRNCLSL EHKSSDSTFLVFMSHGILDGICGTWHSEEEPDVLPYDTIFRTFNNRNCLSL	FHKSTGMTSRSGTDVDAANLRETFRNLKYEVRNK-NDLTREEIVELMRDVSKE FDKVTGMGVRNGTDKDAEALFKCFRSLGFDVIVY-NDCSCAKMQDLLKKASEE KEFNYLHNRNGSELDLLGMRDLLENLGYSVVI KENLTAQEMETALRQFAAHP XEFDHLPPRNGADFDIIMMQELLENLGYSVVI KENLTAQEMETALRQFAAHP TEFDHLPPRNGADFDIIGMKELLEGLDYSVDVEENLTARDMESALRAFATRP T	



#### h\_Caspase-3 FIGURE \_Caspase-4 \_Caspase-5 \_Caspase-12 \_Caspase-2 \_Caspase-9 \_Caspase-10 \_Caspase-6 \_Caspase-5 \_Caspase-13 \_Caspase-12 \_Caspase-7 \_Caspase-2 \_Caspase-10 \_Caspase-8 Caspase-1 Caspase-9 Caspase-8 Caspase-14 Caspase-6 Caspase-1 QNKPKMFFIQACRGDETDRGVDQQDGKN----HAGSPGCEESDAGKE-----KLPKMRL GGKPKLFFIQACGGEQKDHGFEVASTSPEDESPGSNPEPDATPFQEGLRTFDQLDAISSL AEKPKLFFIQACQGEEIQPSVSIEADALN---PEQAPTSLQ------AGKPKVFFIQACQGDNYQKGIPVETDS----EEQPYLEMDLS-----SPQTRYI RNKPKILIMQACRGR--YNGTIWVSTN----KGIATADTDEERVLS---CKWNNSITKA A--HADGDCFVFCILT#GRFG-----AVYSSDE-----ALIPIREIMSHFTALQCPRI D--HSNMDCFICCILS#GDKG----IIYGTDG----QEAPIYELTSQFTGLKCPSL E--HKTSDSTFLVFMS#GIRE-----GICGKKHSEQVPDILQLNAIFNMLNTKNCPSL E--HKSSDSTFLVLMSHGILE-----GICGTAHKKKKPDVLLYDTIFQIFNNRNCLSI VGKPKIFIIQACRGN--QHDVPVIPLDV----VDNQTEKLDTNITEVD-----AASVYTL KDKPKVIIVQACRGE--KHGELWVRDSP----ASLAVISSQSSENLE----ADSVCKI KDKPKVIIVQACRGA--NRGELWVSDSP----PALADSFSQSSENLE-----EDAVYKI KDKPKVIIVQACRGA--NRGELWVRDSP----ASLEVASSQSSENLE-----EDAVYKT KDKPKVIIMQAC\_RGN--GAGIVWFTTD-----SGKASADTHG-RLLQGNIC--NDAVTKA TGKPKLFIIQACRGT--ELDCGIETDSG-----VDDDMAC------DSREDPVSCAFVVLMAHGREG----FLKGEDG----EMVKLENLFEALNNKNCQAL A--HRVTDSCIVALLS**H**GVEG-----AIYGVDG-----KLLQLQEVFQLFDNANCPSI KDKPKVIIIQACRGD--SPGVVWFKDSV----GVSGNLSLPTTEEFE-----DDAIKKA LEKPKLFF1QA**C**RGT--ELDDG1QADSG----P1NDTDANPR------YK1F --HGALDCCVVVILS**H**GCQASHLQFPGAVYGTDG-----CPVSVEKIVNIFNGTSCPSL -HADADCFVCVFLSHGEGN-----HIYAYDA-----KIEIQTLTGLFKGDKCHSL ----HKIP

VDA-DFLYAYSTAPGYYSWRNSKDGSWFIQSLCAMLKQYA-DKLEFMHILTRVNRKVATE
VEA-DFLFAYSTVPGYYSWRSPGRGSWFVQALCSILEEHG-KDLEIMQILTRVNDRVARH
HVEKDFIAFKSSTPHNVSWRHETNGSVFISQIIYYFREYS-WSHHLEEIFQ----KVQHS
HVEKDFIAFKSSTPHNISWKVGKTGSLFISKLIDCFKKYC-WCYHLEEIFR----KVQQS
HVEKDFIAFCSSTPHNVSWRDSTMGSIFITQLITCFQKYS-WCCHLEEVFR----KVQQS
HEEKDFIAFCSSTPHNVSWRDIKKGSLFITELITCFQKYS-CCCHLMEIFR----KVQKS
HIEKDFIAFCSSTPHNVSWRDRTRGSIFITELITCFQKYS-CCCHLMEIFR----KVQKS

h\_Caspase-3

\_Caspase-14

RAKPKVYIIQACRGEQRDPGETVGGDE----IVMVIKDSP-----

\*\*\*: ::\*\*\*

\_Caspase-7

Саяраяе-12

Caspase-12

\_Caspase-4

\_Caspase-13

\_Caspase-5

\_Caspase-1

SEALOSUE GEALO YE HOLD HAMPTAKEN



### FIGURE 4E

h\_Caspase-9 h\_Caspase-2 h\_Caspase-14 h\_Caspase-6 h\_Caspase-8 Caspase-10

PAEADFLLGLATVPGYVSFRHVEEGSWYIQSLCNHLKKLVPRMLKFLEKTM----EIRGR PTPSDIFVSYSTFPGFVSWRDPKSGSWYVETLDDIFEQWA-HSEDLQSLLL----RVANA PDEADFLLGMATVNNCVSYRNPAEGTWYIQSLCQSLRERCPRGDDILTILT----EVNYE PAGADFLMCYSVAEGYYSHRETVNGSWYIQDLCEMLGKYG-SSLEFTELLTLVNRKVSQR PTYTDALHVYSTVEGYIAYRHDQKGSCFIQTLVDVFTKRK---GHILELLT----EVTRR PTRSDMICGYACLKGTAAMRNTKRGSWYIEALAQVFSERA-CDMHVADMLVKVN-ALIKD

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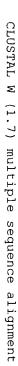
m\_Caspase-12 h\_Caspase-7 h\_Caspase-3 Caspase-14 \_Caspase-4 \_Caspase-10 \_Caspase-1 \_Caspase-6 \_Caspase-13 Caspase-9 \_Caspase-8 Caspase-12 Caspase-2 Caspase-5 RVDFCKDPSAIGKKQVPCFASMLTKK--LHFFPKSN-MAEAELVQEGKARKTNPEIQSTLRKR--LYLQ----VSV-----KGIYKQMPGCFNFLRKK--LFFKTS---VSN--KDDKKNMGKQMPQPTFTLRKK--LVFPSD---FEQ----PDGRAQMPTTERVTLTRCF--YLFPGH---FEV----PQAKAQMPTIERATLTRDF--YLFPGN--FET----PRAKAQMPTIERLSMTRYF--YLFPGN--FESQSDDPHFHEKKQIPCVVSMLTKE--LYFSQ----REGYAPGTEFHRCKEMSEYCSTLCRH-LYLFPGHPPT KRTVWG-AKQISATSLPTAISAQTPRPPMRRWSSVS-FEK----PNVKAQMPTVERLSMTRYF--YLFPGN---FEV----PGELTQMPTIERVSMTRYF--YLFPGN---FET----PNILTQLPTIERLSMTRYF--YLFPGN---FESFSFDATFHAKKQIPCIVSMLTKE--LYFYH---

#### Legend:

- Active-site Residues
- Identical Residues
- Conservative Substitution

Allowable Substitution

Northiti λB SSAJOEUS QB~OMBUY





## FIGURE 5A

h_Caspase-4 h_Caspase-5 h_Caspase-13 h_Caspase-12	h_Caspase-4 h_Caspase-5 h_Caspase-13 h_Caspase-12 h_Caspase-1	h_Caspase-4 h_Caspase-5 h_Caspase-13 h_Caspase-12 h_Caspase-1	h_Caspase-4 h_Caspase-5 h_Caspase-13 h_Caspase-12 h_Caspase-1	h_Caspase-4 h_Caspase-5 h_Caspase-13 h_Caspase-12 h_Caspase-1
YSVDVEENLTARDMESALRAFATRPEHKSSDSTFLVLMSHGILEGICGTVHDEKKPDVLL YTVVDEKNLTARDMESVLRAFAARPEHKSSDSTFLVLMSHGILEGICGTAHKKKKPDVLL YTVEVEEKLTARDMESVLWKFAAREEHKSSDSTFLVFMSHGILDGICGTMHSEEEPDVLP YSVVIKENLTAQEMETALRQFAAHPEHQSSDSTFLVFMSHGILNGICGTKHWDQEPDVLH	HEEFLRLCKERAEEIYPIKERNNRTRLALIICNTEFDHLPPRNGADFDITGMKELLEGLD REEFLRLCKKNHDEIYPIKKREDRRRLALIICNTKFDHLPARNGAHYDIVGMKRLLQGLG HEEFLKLCKERAGEIYPIKERKDRTRLALIICNTEFDHMPPRNGAALDILGMKQLLEGLG HAHFHELKTKRADEIYPVMEKERRTCLALNIRNKEFNYLHNRNGSELDLLGMRDLLENLG LEEAQRIWKQKSAEIYPIMDKSSRTRLALIICNEEFDSIPRRTGAEVDITGMTMLLQNLG	NIDQISPNKKAHPNMEAGPPESGESTDALKLCP N	GKDFLTGVLDNLVEQNVLNWKEEEKKKYYDAKTEDKVRVMADSMQEKQRMAGQMLLQTFF GKDVLHGVFNYLAKHDVLTLKEEEKKKYYDAKIEDKALILVDSLR-KNRVAHQMFTQTLL GKELISGLLDDFVEKNVLKLEEEEKKKIYDAKLQDKARVLVDSIRQKNQEAGQVFVQTFL IKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVDDITETAQIAGKIFREHLM GEGTINGLLDELLQTRVLNKEEMEKVKRENATVMDKTRALIDSVIPKGAQACQICITYIC : : *::: : **:: : : **:: : : **:: : : **:: : **	MFKGILQSGLDNFVINHMLKNNVAGQTSIQTLVPNTDQKSTSVKKDN-HKKKTVKMLEYLMAEGK-HNKNPLKMLEYLMAEDK-HNKNPLKMLESLMAEDK-HNKNPLKMLESL

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SUBCLASS	CLASS	Y8	
:3		CSVORIGA.	



h_Caspase-4 SFEVPQAKAQ h_Caspase-13 SFEKPNVKAQ h_Caspase-12 SFETPNILITQ h_Caspase-1 SFEQPDGRAQ	h_Caspase-4 h_Caspase-5 h_Caspase-13 h_Caspase-13 h_Caspase-12 h_Caspase-1 h_Caspase-1 h_Caspase-1 h_Caspase-1 h_Caspase-1	h_Caspase-4  h_Caspase-5  h_Caspase-13  h_Caspase-12  h_Caspase-12  h_Caspase-1  h_Caspase-1  h_Caspase-1  h_Caspase-1  h_Caspase-1  h_Caspase-1  h_Caspase-1  h_Caspase-1  h_Caspase-1	FIGURE 5B  h_Caspase-1  *:* :::**
SFETPRAKAQMPTIERLSMTRYFYLFPGN SFEVPQAKAQMPTIERATLTRDFYLFPGN SFEKPNVKAQMPTVERLSMTRYFYLFPGN SFETPNILTIQLPTIERLSMTRYFYLFPGN SFEQPDGRAQMPTTERVTLTRCFYLFPGH *** * ; *: ** ** ; : ** ******	DAVYKTHVEKDFIAFCSSTPHNVSWRDSTMGSIFITQLITCFQKYSWCCHLEEVFRKVQQ DSVCKIHEEKDFIAFCSSTPHNVSWRDRTRGSIFITELITCFQKYSCCCHLMEIFRKVQK DAVYKTHVEKDFIAFCSSTPHNVSWRDIKKGSLFITRLITCFQKYAWCCHLEEVFRKVQQ DAVTKAHVEKDFIAFKSSTPHNVSWRHETNGSVFISQIIYYFREYSWSHHLEEIFQKVQH DAIKKAHIEKDFIAFCSSTPDNVSWRHPTMGSVFIGRLIEHMQEYACSCDVEEIFRKVRF *:; * * ****** ************************	YDTIFQIFNNRNCLSLKDKPKVIIVQACRGANRGELWVR-DSPASLEVASSQSSE-NLEE YDTIFQIFNNRNCLSLKDKPKVIIVQACRGEKHGELWVR-DSPASLAVISSQSSE-NLEA YDTIFRTFNNRNCLSLKDKPKVIIVQACRGANRGELWVS-DSPALADSFSQSSE-NLEE DDTIFEIFNNRNCQSLKDKPKVIIMQACRGNGAGI_VWFTTDSGKASADTHGRLLQGNICN LNAIFNMLNTKNCPSLKDKPKVIIIQACRGDSPGVVWFK-DSVGVSGNLSLPTTE-EFED ::**.;** *******************************	YSVDVKKNLTASDMTTELEAFAHRPEHKTSDSTFLVFMSHGIREGICGKKHSEQVPDILQ*:* :::*** : * * : **:*

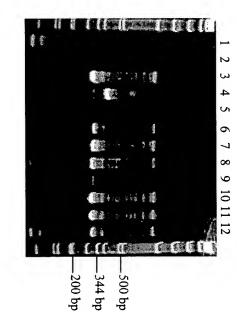
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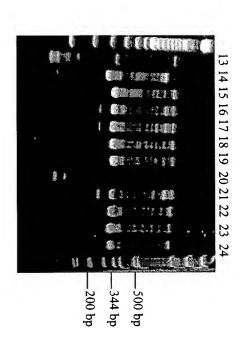
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Active-site Residues

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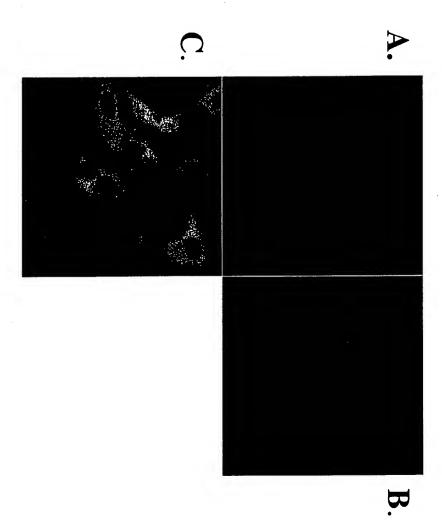




brain 22. Fetal liver 23. Fat 24. Mammary gland 9. Muscle 10. Stomach 11. Testis 12. Placenta 13. Pituitary 14. Thyroid gland 15. Adrenal gland 16. Pancreas 17. Ovary 18. Uterus 19. Prostate 20. PBL 21. Fetal 1. Brain 2. Heart 3. Kidney 4. Spleen 5. Liver 6. Colon 7. Lung 8. Small Intestine

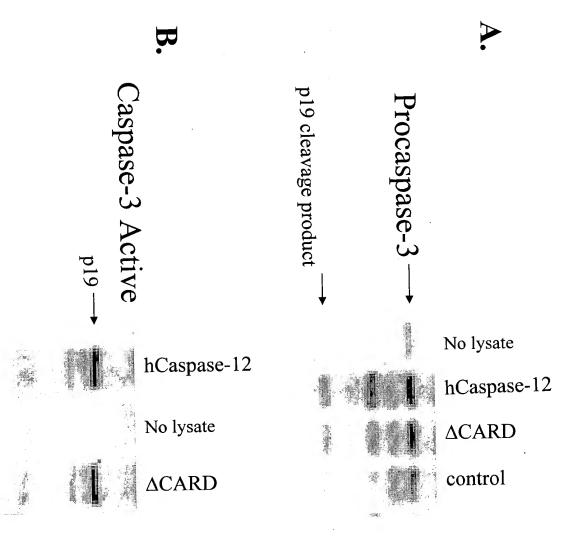
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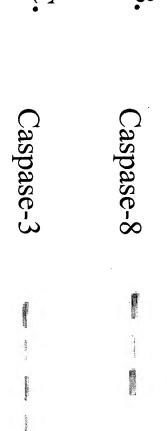
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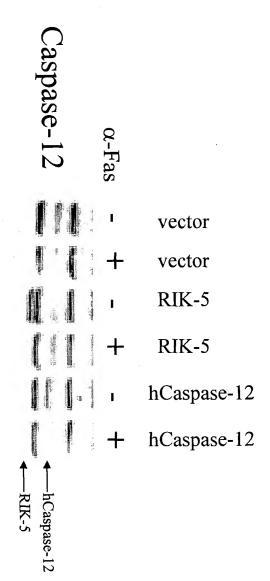




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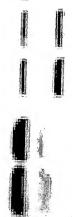
Sekicaus seulo ya

## A23187

 $\beta$ -amyloid

0 40

Hours



Caspase-12 — ~ 49 kDa

Hours

# Tunicamycin

SH-EP

8 16 24

Hours 0

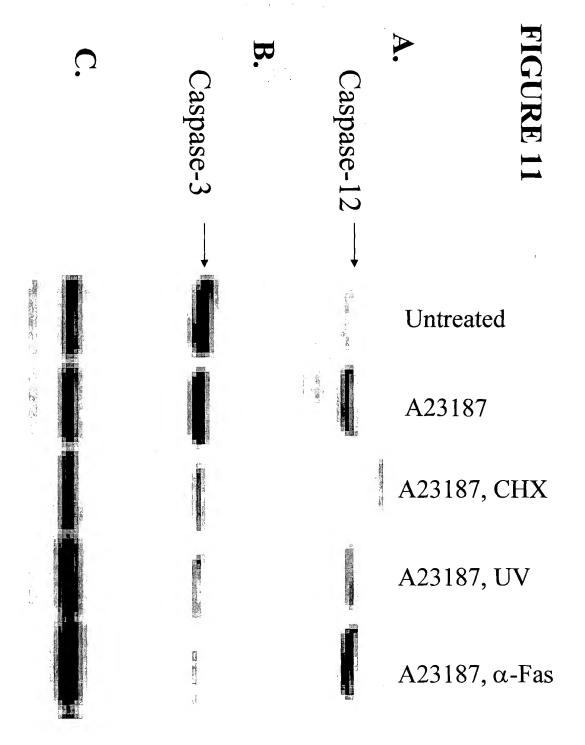
Caspase-12

SH-EP

Hours 0

GRP 78 -

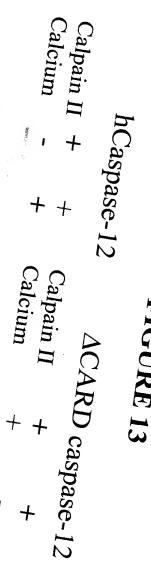






B. Caspase-12 Caspase-3







49 kDa –